ABSTRACT

Polyamine compounds, method of synthesis and method of use for anti-cancer purposes, and for enhancing the activity of existing anti-cancer drugs are provided. This disclosure has identified certain polyamine motifs that can be attached to toxic agents to facilitate their access to cancer cells as well as polyamine compounds of surprising cytotoxicity and selectivity in killing cancer cells. It includes an illustrative conjugate system with examples of a triamine or a tetraamine appended to a cytotoxic agent. There are five method schemes illustrative of the synthesis of the compounds of the invention. Included is a general strategy to enhance cell uptake by attaching a polyamine vectoring system with an example of a triamine vector attached to an existing anti-cancer drug to improve its chemotherapeutic potency. There is an illustration of using the triamine vector to improve the selectivity of an anthracenylmethyl amine cytotoxic agent (e.g. an anthracenylmethyl-4, 4-triamine conjugate outperformed an anthracenylmethyl N-butyl amine derivative). There is an illustration of a synthetic method to attach the polyamine vector onto an existing chemotherapeutic, doxorubicin. This methodology can lead to the synthesis of the polyamine-doxorubicin conjugate. There are illustrations of the synthesis of various alkyl aryl substituted polyamines, a hydroxylated polyamine derivative and a cyclohexyldiamine analogue.